A Small-Molecule Wnt Mimic Improves Human Limbal Stem Cell Ex Vivo Expansion.

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Public Summary:
In this study, a small molecule that activates Wnt signaling was generated and applied to the ex vivo cultivation of the stem cells of the cornea. Wnt signaling is a specific type of signaling among cells that plays a role in the maintenance of stem cells. This Wnt small molecule helped in the maintenance and expansion of the corneal stem cells. The small molecules generated in this study may be helpful in the development of pharmaceutical reagents for treating corneal wounds.

Scientific Abstract:
Ex vivo cultured limbal stem/progenitor cells is an effective alternative to other surgical treatments for limbal stem cell deficiency, but a standard xenobiotic-free method for culturing the LSCs in vitro needs to be optimized. Because Wnt ligands are required for LSC expansion and preservation in vitro, to create a small-molecule Wnt mimic, we created a consolidated compound by linking a Wnt inhibitor that binds to the Wnt co-receptor Frizzled to a peptide derived from the N-terminal Dickkopf-1 that binds to Lrp (low-density lipoprotein receptor-related protein) 5/6, another Wnt co-receptor. This Wnt mimic not only enhances cellular Wnt signaling activation, but also improves the progenitor cell phenotype of in vitro cultured limbal epithelial cells. As the maintenance of stem cell characteristics in the process of culture expansion is essential for the success of ocular surface reconstruction, the small molecules generated in this study may be helpful in the development of pharmaceutical reagents for treating corneal wounds.